

- wherein a group comprises sequencing reads from one of the uniquely labeled double-stranded target nucleic acid molecules; and
- (e) comparing the first-strand sequencing reads with the second-strand sequencing reads in each group, and generating an error-corrected sequence for a plurality of the double-stranded target nucleic acid molecules by distinguishing erroneous nucleotides in one strand that lack a matched base change in the complementary strand.
- 40.** The method of claim **39**, wherein the double-stranded cyphers comprise random identifier sequences.
- 41.** The method of claim **39**, wherein the double-stranded cyphers comprise identifier sequences that are not completely random.
- 42.** The method of claim **39**, wherein a target tag sequence comprises nucleotides at an end of a target nucleic acid molecule.
- 43.** The method of claim **42**, wherein the end of the target nucleic acid molecule is a sheared end.
- 44.** The method of claim **39**, wherein the random or partially-random identifier sequence is double-stranded.
- 45.** The method of claim **39**, wherein the identifier sequence is at an end of the double-stranded cypher.
- 46.** The method of claim **39**, wherein the target tag sequence is 5 nucleotides to 20 nucleotides in length.
- 47.** The method of claim **39**, wherein each of the cyphers are unique.
- 48.** The method of claim **39**, wherein the erroneous nucleotides comprise a polymerase error that arose during amplification or sequencing.
- 49.** The method of claim **39**, wherein the plurality of target nucleic acid molecules comprise a mutation present at a frequency of  $2.1 \times 10^{-6}$  or lower.
- 50.** The method of claim **39**, further comprising detecting a cancer biomarker in one of the error-corrected sequences, wherein the cancer biomarker comprises a nucleotide mutation.
- 51.** The method of claim **39**, further comprising using the error-corrected sequences to assess cancer response to therapy.
- 52.** The method of claim **39**, wherein the sample is derived from a human subject having cancer, and wherein the method further comprises detecting in one of the error-corrected sequences a mutation that confers to the cancer resistance to cancer therapy.
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